Δ Vancomycin Powder Reduces Infection in an Open Fracture Model

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Background/Purpose: Use of locally applied vancomycin powder as a surgical adjunct to decrease surgical site infections has garnered increased attention in the spine literature where its use led to a 4-fold decrease in deep infections. The impact of this on the orthopaedic trauma community is largely unknown because spine infections are generally considered surgical site infections where bacteria are introduced at the time of surgery. However, open fractures are often contaminated at the time of injury, followed by early surgical intervention. Traditionally, a delivery device, such as polymethylmethacrylate (PMMA), has been used for local antibiotic application as it elutes antibiotic over time, but this requires an additional procedure for removal. The use of vancomycin powder allows for local antibiotic application that can be distributed throughout the wound and cleared by the body without the need for surgical removal. However, there is concern that its potential rapid disappearance from the wound would make it less effective in the setting of an open fracture. The purpose of this study was to determine if locally applied vancomycin powder in an established contaminated rat femoral defect model would decrease the incidence of infection.

Methods: Critical size (6 mm) defects were created in 40 Lewis rat femurs and supported by a polyacetyl plates and threaded Kirschner wires. Each animal was inoculated with 105 colony-forming units (CFU) of UAMS-1, a Staphylococcus aureus osteomyelitis isolate, at the time of surgery via a collagen matrix. The animals were then assigned to one of three groups: debridement and irrigation (D&I) without local antibiotics (Standard Treatment), D&I with vancomycin-loaded (10% wt/wt) PMMA beads (Vanc Beads), or D&I with 50 mg local vancomycin powder (Vanc Powder), which is a sufficient application to coat the entirety of the wound bed prior to closure. They were randomized for treatment at either 6 or 24 hours postinoculation, when the wound was then reopened, debrided, and irrigated with saline and the treatment applied. Every animal received 72 hours of twice daily cefazolin (5 mg/kg) beginning at the time of debridement. Serum antibiotic levels were measured at 24 hours, 7 days, and 14 days. All animals survived for 14 days post treatment. Following euthanasia, bacteria were quantified and local inflammatory markers (interleukin [IL]-6, TNFα [tumor necrosis factor alpha], and RANTES) were measured.

Results: Locally applied vancomycin powder effectively reduced bacteria both within the bone (Figure 1A) and on the hardware (Figure 1B) when treatment was not delayed ($P<0.001$). Furthermore, there were similar results for the Vanc Powder and Vanc Beads groups at both time points. Interestingly, neither of the local antibiotic strategies reduced infection rates when treatment was delayed until 24 hours. The inflammatory markers corresponded with the bacteria levels in all groups at each treatment time point (data not shown). Vancomycin was detectable in the blood of all Vanc Powder animals at 24 hours post administration with an average of 10.30 μg/mL. At 7 days, the serum antibiotic levels averaged 0.13 μg/mL and were present in only 30% of Vanc Powder animals. By day 14, only 20% of Vanc Powder

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See pages 47 - 108 for financial disclosure information.

animals had detectable serum levels of antibiotic, averaging less that 0.05 $\mu g/mL$. At each time point there was no vancomycin detectable in the serum of the Vanc Beads animals.

Conclusion: This study suggests that vancomycin powder is a promising adjunctive therapy for preventing infection in traumatic wounds if treatment is not delayed. This time-dependent effectiveness of vancomycin powder is similar to what has been observed with both systemic and other local delivery adjuncts due to rapid biofilm formation occurring within a few hours of contamination, making the bacteria recalcitrant to antimicrobials. Similar to what has been reported by the spine community, vancomycin powder may be particularly useful for infection prevention when used in early primary closure of traumatic wounds.

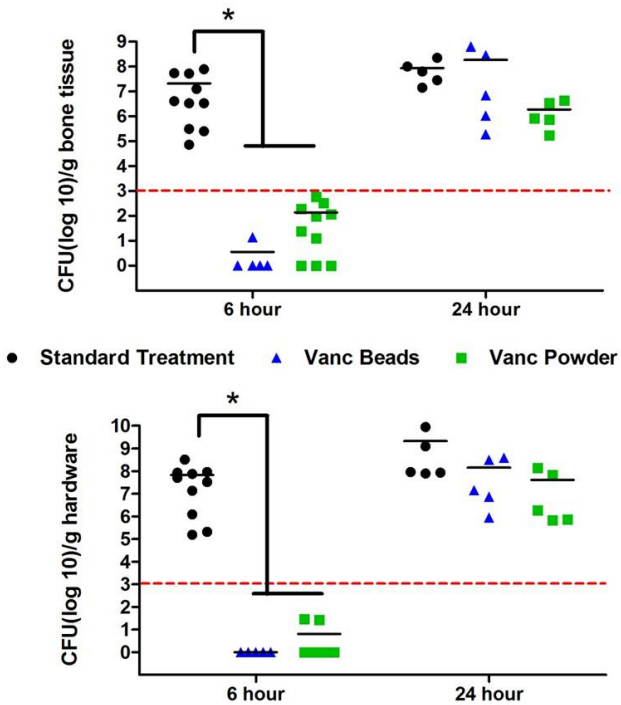

Figure 1. Effect of vancomycin treatment type and time on limb infection. (A) Bacterial count within the bone; (B) Bacterial count on the hardware. Significant difference between those infected (CFU > 10^3) and not infected (CFU < 10^3)(red line) at 6 hours ($P<0.001$) but not at 24 hours ($p=1$) (Fisher's Exact Test)